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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/964,042	09/26/2001	Ralph Weichselbaum	27373/36638A	1056

4743 7590 02/07/2008

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

MAIL DATE	DELIVERY MODE
02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/964,042	WEICHSELBAUM ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,10-13 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 10-13, 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/15/2007 has been entered.

Claims 1-5, 10-13, 16 are currently pending in the application and are addressed herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 10-13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Advani (1997; Int. Journ. Oncol. Rad. Biol. Phys, previously of record) in view of Carroll et al. (Ann. Surg. 1996, previously of record).

The instant claims are drawn to a method for reducing a non-central nervous system tumor mass by administering a therapeutically effective amount of an attenuated HSV to a subject having cancer wherein the HSV genome has been modified in an inverted repeat region such that the HSV has only one active gamma(1)34.5 gene, wherein the HSV is administered in an amount effective to reduce the mass of the tumor mass.

Advani (1997) is an abstract that teaches "Human U-87MG glioma cells were grown in the hind limb of athymic mice... and infected with... [HSV] R7020... the tumors were harvested... 14 days after viral injection." Furthermore, Advani teaches, "Herein we demonstrate radiation enhanced viral replication as one of the interactive effects of combining IR and attenuated HSV in treating glioma xenografts and a potential therapeutic motif in the treatment of gliomas." Therefore, Advani (1997) clearly teaches a method for reducing tumor mass comprising direct delivery of the attenuated HSV (HSV R7020) to the tumor.

Advani does not explicitly teach that the attenuated HSV R7020 virus could be used to treat a non-CNS tumor in vivo, nor does Advani teach the particular amount of the HSV which would be a therapeutically effective amount for reducing tumor mass.

Carroll teaches treatment of non-CNS tumor using an attenuated HSV (hrR3). Specifically, Carroll teaches a method for treating colon carcinoma liver metastasis by administering an attenuated HSV directly to cells the tumor (e.g., see abstract).

Therefore, it would he been prima facie obvious at the time of invention that the method taught by Advani would have also been able to treat a non-CNS tumor such as a colon carcinoma liver metastasis in an animal or human, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to modify the method of Advani to treat a non-CNS cancer because Carroll teaches that attenuated HSVs can be used to treat non-CNS-type tumors. Furthermore, the in vitro findings that taught by the Advani references are indicative of an expectation of success for directly administering the vectors to tumors in vivo. Furthermore, it would have been prima facie obvious to perform routine optimization to find the amount of HSV which would be a therapeutically effective amount for reducing tumor mass. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Therefore, routine optimization is not considered inventive, and considering the teaching of Advani that IR treatment augments HSV replication, which would increase the HSV's antitumor activity, it would have been routine to identify the optimum amount for treating tumors.

Response to Arguments

Applicant's arguments filed 2/21/2007 have been fully considered, but are not persuasive.

Applicants argue that Advani is fails to teach or suggest using an HSV to treat non-CNS tumors and fails to teach or suggest a therapeutically effective amount of a claimed HSV because Advani fails to teach that HSV R7020 is useful in reducing non-CNS tumor mass or any tumor mass. Applicants assert that Advani does not disclose data establishing a reduction in tumor mass and does not teach a therapeutically effective amount of an HSV for use in reducing tumor mass. Applicants argue that Advani does not provide an enabling disclosure of administering an HSV in an amount to reduce tumor mass. Applicants argue that Carroll does not remedy the deficiencies of Advani and asserts that Carroll has been improperly generalized because Carroll teaches the use of an attenuated HSV not encompassed by the claims.

In response, it is noted that Advani was testing whether or not IR treatment could augment the tested HSV replication, which Advani indicates would increase the anti-tumor effect of the virus. Advani demonstrates an increase in viral replication when IR is used in combination with the HSVs, indicating that at least for the period of time that the virus is replicating, the viral replication would be treating the tumor which would at least slow the growth of the tumor, thus resulting in a reduction of the tumor mass compared to untreated tumors. Specifically, Advani teaches, "[the results] demonstrate radiation enhanced viral replication as one of the interactive effects of combining IR and attenuated HSV in treating glioma xenografts and a potential therapeutic motif in the treatment of gliomas" (emphasis added). This is a clear indication that the treatment is useful for "treating" glioma tumors, where

"treating" would be a decrease in tumor mass compared to untreated tumors. Furthermore, considering that IR treatment augments HSV replication (as taught by Advani), which would increase the HSV's antitumor activity, it would have been routine to identify the optimum amount for treating tumors. With respect to the Carroll reference, it is acknowledged that Carroll does not teach an attenuate HSV encompassed by the instant claims. However, as previously indicated, Advani teaches that the claimed attenuated HSV can be used to treat CNS tumors, but is silent with respect to non-CNS tumors. Furthermore, Carroll teaches that an attenuated HSV, albeit a non-claimed HSV, can treat non-CNS tumors. Therefore, there would have been at least a motivation to try using the attenuated HSVs of Advani to treat non-CNS tumors, and given the results of both Advani and Carroll there would have been a reasonable expectation of success. The Examiner respectfully disagrees with the assertion that the teaching of Carroll has been improperly generalized. It is acknowledged that Carroll does not teach a claimed HSV, but Carroll does teach an attenuated HSV can be used to treat a non-CNS tumor. Furthermore, Advani teaches that the claimed attenuated HSV can be used to treat CNS tumors. Additionally, there is no evidence of record indicating why there would not be a reasonable expectation that the claimed HSV could treat non-CNS tumors. In other words, since the claims HSV can treat CNS tumors, and considering that an attenuated HSV was known to treat non-CNS tumors (Carroll) and in absence of any evidence that one of skill in the art would doubt that the claimed HSV would be able to treat non-CNS tumors, one of ordinary skill in the art would reasonably expect that the claimed HSV would treat CNS tumors as well as non-CNS tumors.

Therefore, Applicants arguments are not persuasive.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner
Art Unit 1635